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Atty. Dkt. No. 029488-0112

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Jay BUA  
Title: REDUCTION OF BREAST DENSITY WITH  
4-HYDROXY TAMOXIFEN  
Appl. No.: 10/734,644  
Filing Date: 12/15/2003  
Examiner: Not yet assigned  
Art Unit: 1645

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicant in order to comply with Applicant's duty of disclosure pursuant to 37 CFR §1.56. A copy of each listed document is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.



**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

**RELEVANCE OF EACH DOCUMENT**

The relevance of the foreign-language documents is described in the present specification. An English translation of the foreign-language documents is not readily available. However, the absence of such translation does not relieve the PTO from its duty to consider the submitted foreign language documents (37 CFR §1.98 and MPEP §609).

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date 16 June 2004

By S. A. Bent

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### U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			

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### NON PATENT LITERATURE DOCUMENTS

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	A1	Charlotte ATKINSON et al., "Mammographic Patterns as a Predictive Biomarker of Breast Cancer Risk: Effect of Tamoxifen", Cancer Epidemiology, Biomarkers & Prevention, Vol. 8, October 1999, pp. 863-866.	
	A2	J. BARRAT et al., "Effet <i>in vivo</i> de l'administration locale de progestérone sur l'activité mitotique des galactophores humains", J. Gynecol. Obstet. Biol. Reprod. 19: 269-274 1990.	
	A3	N.F. BOYD et al., "Relationship Between Mammographic and Histological Risk Factors for Breast Cancer", Journal of the National Cancer Institute, Vol. 84, No. 15, August 5, 1992, pp. 1170-1179.	
	A4	N.F. BOYD et al., "Quantitative Classification of Mammographic Densities and Breast Cancer Risk: Results from the Canadian National Breast Screening Study", Journal of the National Cancer Institute, Vol. 87, No. 9, May 3, 1995, pp. 670-675.	
	A5	Norman F. BOYD et al., "Effects at Two Years of a Low-Fat High-Carbohydrate Diet on Radiologic Features of the Breast: Results from a Randomized Trial", Journal of the National Cancer Institute, Vol. 89, No. 7, April 2, 1997, pp. 488-496.	
	A6	Jacques BRISSON et al., "Tamoxifen and Mammographic Breast Densities", Cancer Epidemiology, Biomarkers & Prevention, Vol. 9, September 2000, pp. 911-915.	
	A7	Bronaugh & Maibach, "Percutaneous Absorption Drugs-Cosmetics-Mechanisms-Methodology", Marcel Dekker Inc., New York, 1999.	

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	A8	Celia BYRNE, "Studing Mammographic Density: Implications for Understanding Breast Cancer", Journal of the National Cancer Institute, Vol. 89, NO. 8, April 16, 1997, pp. 531-537.	
	A9	Philip CARTHEW et al., "Cumulative exposure to tamoxifen: DNA adducts and liver cancer in the rat", Arch Toxicol (2001) 75: 375-380.	
	A10	Gerard CHETRITTE et al., "Effect of Promegestone, Tamoxifen, 4-Hydroxytamoxifen and ICI 164,384 on the Oestrone Sulphatase Activity of Human Breast Cancer Cells", Anticancer Research 13: 931-934 (1993).	
	A11	Eric C. DIETZE et al., "Tamoxifen but Not 4-Hydroxytamoxifen Initiates Apoptosis in p53(-) Normal Human Mammary Epithelial Cells by Inducing Mitochondrial Depolarization", The Journal of Biological Chemistry Vol. 276, No. 7, Issue of February 16, 2001, pp. 5384-5394.	
	A12	Laurie L. FAJARDO MD et al., "Correlation Between Breast Parenchymal Patterns and Mammographers' Certainty of Diagnosis", Investigative Radiology, Vol. 23, No. 7, July 1988, pp. 505-508.	
	A13	Ian S. FENTIMAN, "Tamoxifen and Mastalgia an Emerging Indication", Drugs, Vol. 32, No. 6, December 1986, pp. 477-480.	
	A14	I.S. FENTIMAN et al., "Dosage and duration of tamoxifen treatment for mastalgia: a controlled trial", BR. J. SURG. September 1988, Vol. 75, No. 9, pp. 845-846.	
	A15	I.S. FENTIMAN et al., "Studies of tamoxifen in women with mastalgia", The British Journal of Clinical Practice, Supplement 68, Vol. 43, No. 11, November 1989, pp. 34-36.	
	A16	N. GIAMBIAGI et al., "IMMUNOLOGICAL DIFFERENCES BETWEEN THE ESTRADIOL-, TAMXIFEN- AND 4-HYDROXY-TAMOXIFEN-ESTROGEN RECEPTOR COMPLEXES DETECTED BY TWO MONOCLONAL ANTIBODIES", J. Steroid Biochem. Vol. 30, No. 1-6, pp. 213-217, 1988.	

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	A17	Susan C. HARVEY et al., "Marked Regression of a Nonpalpable Breast Cancer After Cessation of Hormone Replacement Therapy", American Journal of Roentgenology, August 1996, 167: 394-395.	
	A18	Jennifer A. HARVEY et al., "Short-term Cessation of Hormone Replacement Therapy and Improvement of Mammographic Specificity", Journal of the National Cancer Institute, Vol. 89, No. 21, November 5, 1997, pp. 1623-1625.	
	A19	IBIS investigators, "First results from the International Breast Cancer Intervention Study (IBIS-I): a randomised prevention trial", The Lancet, Vol. 360, September 14, 2002, pp. 817-824.	
	A20	Susan JENKS, "Dense Breast Tissues May Hold Increased Cancer Risk for Some", Journal of the National Cancer Institute, Vol. 86, No. 8, April 20, 1994, pp. 578-580.	
	A21	V. Craig JORDAN et al., "Metabolites of tamoxifen in animals and man: identification, pharmacology, and significance", Breast Cancer Research and Treatment, 2, pp. 123-138.	
	A22	Karla KERLIKOWSKE MD et al., "Effect of Age, Breast Density, and Family History on the Sensitivity of First Screening Mammography", JAMA, vol. 276, No. 1, July 3, 1996, pp. 33-38.	
	A23	Z. KAUFMAN et al., "The Mammographic Parenchymal Patterns of Women on Hormonal Replacement Therapy", Clinical Radiology (1991), 43, 389-392.	
	A24	Thomas M. KOLB MD et al., "Comparison of the Performance of Screening Mammography, Physical Examination, and Breast US and Evaluation of Factors that Influence Them: An Analysis of 27,825 Patient Evaluations", Radiology, Vol. 225, No. 1, October 2002, pp. 165-175.	
	A25	George G.J.M. KUIPER et al., "Comparison of the Ligand Binding Specificity and Transcript Tissue Distribution of Estrogen Receptors $\alpha$ and $\beta$ ", Endocrinology, Vol. 138, No. 3, 1997, pp. 863-870.	

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	A26	Frédérique KUTTENN et al., "MÉDECINE ET THÉRAPEUTIQUE", C.R. Acad. Sc. Paris, , Série III, No. 12, 1985, 300:457-461.	
	A27	Winnie LEUNG MD et al., "Mammographic density in women on postmenopausal hormone replacement therapy", SURGERY, Vol. 122, No. 4, October 1997, pp. 669-674.	
	A28	L. MA et al., "Case-Control Study of Factors Associated With Failure to Detect Breast Cancer by Mammography", Journal of the National Cancer Institute, Vol. 84, No. 10, May 20, 1992, pp. 781-784.	
	A29	Catherine MALET et al., "Tamoxifen and Hydroxytamoxifen Isomers <i>versus</i> Estradiol Effects on Normal Human Breast Cells in Culture", Cancer Research, Vol. 48, No. 24, December 15, 1988, pp. 7193-7199.	
	A30	Pierre MAUVAIS-JARVIS et al., "trans-4-Hydroxytamoxifen Concentration and Metabolism after Local Percutaneous Administration to Human Breast", Cancer Research, Vol. 46, March 1986, pp. 1521-1525.	
	A31	Henri PUJOL et al., "Phase I Study of percutaneous 4-hydroxy-tamoxifen with analyses of 4-hydroxy-tamoxifen concentrations in breast cancer and normal breast tissue", Cancer Chemother. Pharmacol., 36:493-498 (1995).	
	A32	Lawrence H. BLOCK PhD "Epidermal and Transdermal Drug Delivery", The Science and Practice of Pharmacy, Medicated Topicals, pp. 836-857 (2000).	
	A33	David W. ROBERTSON et al., "Synthesis of the E and Z Isomers of the Antiestrogen Tamoxifen and Its Metabolite, Hydroxytamoxifen, in Tritium-Labeled Form", J. Org. Chem., 1982, Vol. 47, No. 12, pp. 2387-2393.	
	A34	David W. ROBERTSON et al., "TAMOXIFEN ANTIESTROGENS, A COMPARISON OF THE ACTIVITY, PHARMACOKINETICS, AND METABOLIC ACTIVATION OF THE CIS AND TRANS ISOMERS OF TAMOXIFEN" Journal of Steroid Biochemistry, Vol. 16, pp. 1-13, (1982).	

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	A35	Carolyn M. RUTTER, PhD et al., "Changes in Breast Density Associated With Initiation, Discontinuation, and Continuing Use of Hormone Replacement Therapy", JAMA, Vol. 285, No. 2, January 10, 2001, pp. 171-176.	
	A36	Audrey F. SAFTLAS et al., MAMMOGRAPHIC PARENCHYMAL PATTERNS AND BREAST CANCER RISK", Epidemiologic Reviews, Vol. 9, 1987, pp. 146-174.	
	A37	Fabrice SAUVEZ et al., "Cutaneously applied 4-hydroxytamoxifen is not carcinogenic in female rats", Carcinogenesis Vol. 20, No. 5, pp. 843-850 1999.	
	A38	Hong Ju SON et al., "Significance of Follow-Up Mammography in Estimating the Effect of Tamoxifen in Breast Cancer Patients Who Have Undergone Surgery", American Journal of Roentgenology, 173: 905-909 (1999).	
	A39	Darcy V. SPICER et al., "Changes in Mammographic Densities Induced by a Hormonal Contraceptive Designed to Reduce Breast Cancer Risk", Journal of the National Cancer Institute, Vol. 86, No. 6, March 16, 1994, pp. 431-436.	
	A40	Giske URSIN et al., The Detection of Changes in Mammographic Densities", Cancer Epidemiology, Biomarkers & Prevention, Vol. 7, January 1998, pp. 43-47.	
	A41	John N. WOLFE MD, "RISK FOR BREAST CANCER DEVELOPMENT DETERMINED BY MAMMOGRAPHIC PARENCHYMAL PATTERN", Cancer, May 1976, Vol. 37, No. 5, pp. 2486-2492.	
	A42	Ashini L. WIJAYARATNE et al., Comparative Analyses of Mechanistic Differences Among Antiestrogens", Endocrinology, Vol. 140, No. 12, pp. 5828-5840.	

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